

Title: Adapting Cochrane Diagnostic Test Accuracy Protocol to Toxicological Tests Assessment and a Pilot for Evidence-Based Approach to Two Developmental Toxicity Tests

Evidence-based medicine has been a very defined approach to use systematic review to assess the efficacy of interventions, as pioneered by the Cochrane collaboration. In the safety sciences, evidence-based approaches and their core tool, systematic review (SR), are gaining momentum to enable the evaluation and integration of safety evidence in a transparent and unbiased manner. Potential applications include assessing the safety of environmental chemicals, food ingredients, and regulatory decision-making, and also the comparison and validation of tests methods. The Evidence-Based Toxicology Collaboration ([EBTC](#)) has been established to apply the Cochrane principles of systematic review to toxicology. Challenges and lessons learned from a SR of two toxicity test methods (zebrafish embryological toxicity and prenatal developmental toxicity tests) will be presented. OECD Test Guideline 414 (Prenatal Developmental Toxicity) in small mammals is currently mandated by various regulatory regimes for chemicals registration. EU REACH legislation has created a bottleneck in testing of chemicals for registration as potential developmental hazards. This is being addressed by a few alternative approaches using different decision trees and relying on various combinations of other mammalian OECD test guidelines (TGs). Here, the Zebrafish Embryological Toxicity test (ZET) is being investigated for the first time as a possible alternative to the OECD TG 414 by the authors, using EBT approach. We performed a systematic review of the literature that uses the ZET (the index test) to screen panels of chemicals, including pharmaceutical drugs, industrial and environmental chemicals. These results, after assessment and comparison for methodological performance, were then compared with the results of OECD TG 414 (comparator test). The protocol, literature and database search strategies for this SR will be presented, and the applicability of SRs to the assessment of the performance of other tests will be discussed.